Summary of Safety and Effectiveness Data
Guidant PULSAR™/PULSAR Max™ Pacemaker (D970003)

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PULSAR™/PULSAR Max™ Pacemaker

Guidant Corporation

1 General Information

Device Generic Name:	Implantable Pacemaker Pulse Generator
Device Trade Name:	• Guidant PULSAR™ Models 470, 970, 972, 1172, 1272 Pulse Generators • Guidant PULSAR Max™ Models 1170, 1171, 1270 Pulse Generators • Guidant CONSULT™ (Model 2890) Software
Applicant's Name and Address:	Guidant Corporation Cardiac Pacemakers (CPI) 4100 Hamline Ave. North St. Paul, MN 55112
Product Development Protocol (PDP) Number:	D970003
Date of Notice of Approval to the Applicant:	June 3, 1999

2 Indications and Usage

Guidant PULSAR™/PULSAR Max™ series pacemakers are indicated for the following:

- Symptomatic paroxysmal or permanent second or third-degree AV block
- Symptomatic bilateral bundle branch block
- Symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders (e.g., sinus bradycardia, sinus arrest, sinoatrial [SA] block)
- Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmias
- Neurovascular (vasovagal) syndromes or hypersensitive carotid sinus syndromes

Adaptive-rate pacing is indicated for patients who may benefit from increased pacing rates concurrent with increases in minute ventilation and/or level of physical activity.

The PULSAR™/PULSAR Max™ series pacemakers' dual chamber and atrial tracking modes are also indicated for patients who may benefit from maintenance of AV synchrony. Dual chamber modes are specifically indicated for treatment of the following:

- Conduction disorders that require restoration of AV synchrony, including varying degrees of AV block
- VVI intolerance (e.g., pacemaker syndrome) in the presence of persistent sinus rhythm
- Low cardiac output or congestive heart failure secondary to bradycardia

3 Contraindications

Guidant PULSAR™/PULSAR Max™ pacemakers are contraindicated for the following applications:

- Patients with unipolar pacing leads or in MV mode with an implanted cardioverter-defibrillator (ICD), because it may cause unwanted delivery or inhibition of ICD therapy.
- MV mode in patients with unipolar ventricular leads.
- Single-chamber atrial pacing in patients with impaired AV nodal conduction.
- Atrial tracking modes for patients with chronic refractory atrial tachyarrhythmias (atrial fibrillation or flutter), which might trigger ventricular pacing.
- Dual-chamber and single-chamber atrial pacing in patients with chronic refractory atrial tachyarrhythmias.
- Asynchronous pacing in the presence (or likelihood) of competition between paced and intrinsic rhythms.

4 Warnings and Precautions

See WARNINGS AND PRECAUTIONS in the final draft labeling (Information for Use)

5 Device Description

The Guidant PULSAR™/PULSAR Max™ (hereinafter referred to as PULSAR) pacemakers are multi-programmable, rate-responsive, implantable pacemakers. Two sensors are available with the PULSAR adaptive-rate models: minute ventilation (MV) detection and an accelerometer (motion sensor). These sensors adapt the pacing rate to the patient's changing minute ventilation and activity level. Minute ventilation responds to changes in respiration, and the accelerometer responds to patient activity (motion). PULSAR adaptive-rate models can use either the accelerometer or MV sensor; PULSAR Max models offer a blend of both accelerometer and minute ventilation.

The following models are available. All models listed below feature IS-1 compatible connectors that accept both IS-1 and 3.2 mm leads.

- PULSAR Models 470 (SSI), 970 and 972 (DDD), and 1172 (SR) and 1272 (DR)
- PULSAR Max Models 1170 and 1171(SR), and 1270(DR)

Models 1172, 1272, 1170, 1171, and 1270 require a bipolar ventricular lead when the pacemaker is programmed to use the minute ventilation sensor, either in MV only or blended sensor modes.

The PULSAR pacemaker family can be interrogated and programmed using the Model 2901 Programmer/Recorder/Monitor (PRM) equipped with the Model 2890 software. This software allows the

user to view and change all programmable parameters to optimize the therapy, and to access the diagnostic information stored in the pacemaker.

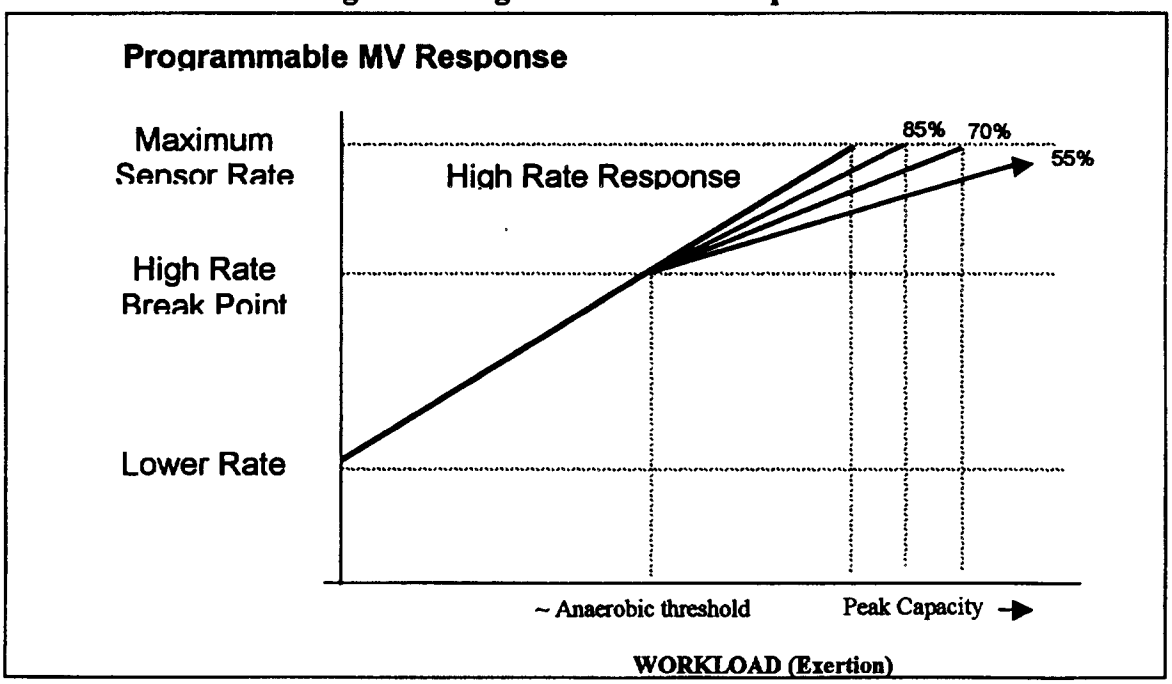
Minute Ventilation (MV)

The PULSAR pacemaker series uses transthoracic impedance to indirectly measure minute ventilation (respiratory rate and tidal volume). To obtain an MV measurement, the device drives a constant current excitation waveform between the ring electrode on the ventricular lead and the pacemaker can. The application of the current between the ring electrode and the can will create an electrical field across the thorax. This electrical field is modulated by respiration. Transthoracic impedance increases during inspiration and decreases during expiration. The device will detect the resulting voltage modulations between the lead tip electrode and the indifferent electrode located on the pacemaker header.

Based on the minute ventilation measurement, the pacemaker calculates a sensor indicated rate by comparing a baseline or resting MV measurement (two hour average) to a short term measurement (30 second average) to determine the change in minute ventilation above rest. This increase in minute ventilation above rest is used to increase the sensor rate in proportion to increases in minute ventilation.

The MV sensor in the PULSAR pacemaker series utilizes several programmable parameters to allow the sensor indicated rate to mimic the heart's natural curvilinear response to increased workload. These parameters are High Rate Break Point and High Rate Response Factor, which operate in conjunction with the Lower Rate Limit (LRL) and the Maximum Sensor Rate (MSR) as illustrated below. The graph illustrates that the programmable dual-slope response can be adjusted so that the programmed MSR will be reached in conjunction with the patient reaching desired peak workload.

Figure 1. Programmable MV Response



Accelerometer

The PULSAR/PULSAR Max adaptive-rate pacemakers sense body motion by means of an integrated circuit accelerometer located on the hybrid assembly. The accelerometer responds to activity in the frequency range of typical physiologic activity (1-10 Hz). An algorithm translates the measured acceleration in this range into a rate increase above the Lower Rate Limit, based on selected values for

several programmable parameters. Because the accelerometer is not in contact with the pacemaker case, response to pressure applied to the pacemaker is negligible.

Dual Sensor Blending

Whenever both adaptive-rate sensors are selected for adaptive-rate pacing, the PULSAR Max pacemaker will blend the two sensor-indicated rates to produce a rate-dependent weighted average response. As a result, the blended response will always be equal to or between the two individual responses.

Whenever the accelerometer response is less than the MV response, the sensor blending will be 100% MV based. If the accelerometer response is greater than the MV response, the blending will range from 80% accelerometer and 20% MV when the blended rate is at LRL, to 40% accelerometer and 60% MV when the blended rate is at MSR.

6 Alternative Practices and Procedures

Cardiac pacing is the standard of care for the indications described above. Other commercially available single chamber or dual chamber pacemakers provide alternatives to the Guidant PULSAR Series pulse generators. Surgery or drug therapy may be alternatives to cardiac pacing in certain instances.

7 Marketing History

The Guidant PULSAR Series pacemakers are currently distributed commercially outside the United States. Specifically, this product is approved for sale in the European Community. As of January 1999, over 1,590 Guidant PULSAR Series devices have been sold and/or implanted outside the United States. This device has not been withdrawn from the market in any country for any reason related to the safety and effectiveness of the device.

8 Adverse Events

Will be the same as the final product labeling.

9 Summary of Preclinical Studies

Studies including laboratory testing, animal testing, and human clinical evaluations have been performed to demonstrate that the PULSAR/PULSAR Max series pacemakers meet performance requirements and are safe and effective. These studies are summarized below.

9.1 Nonclinical Laboratory Studies

System Hazard Analysis

This analysis was performed to identify potential hazards associated with the use of the PULSAR and PULSAR Max pacemaker systems. The pacemaker systems include the implantable pulse generator, the Model 2890 Software Application, and the commercially available Model 2901 or Model 2950 Programmer/Recorder/Monitor (PRM) with the Model 2909 Multiple Application Utility (MAU). The system hazard analysis addressed potential hazards that may result in harm or risk to the patient, operator of the equipment, or other personnel using the PULSAR or PULSAR Max pacemaker systems. Identified potential hazards were documented along with the response taken to control the risk or reduce the effects of the hazard.

Battery Qualification

A component qualification was performed on the batteries used in the PULSAR and PULSAR Max devices to ensure the battery supplier was capable of providing components that meet Guidant requirements. Thirty-nine (39) units were tested. All units were found to operate according to specification. Dimensional Testing was performed by Guidant. Reliability qualification testing (listed below) was performed by the supplier (WGL):

- Non-Destructive Examinations
- Environmental and Safety Tests
- Destructive Analysis
- Electrical Tests

Accelerometer Qualification

A component qualification was performed for the accelerometer used in the PULSAR and PULSAR Max devices to ensure the supplier was capable of providing components that meet Guidant requirements. Seventy-three (73) units were tested. All units were found to operate according to specification. The following tests were performed:

- Electrical Test
- R-C Test
- Centrifuge Test
- Physical Dimensions
- External Visual
- Mechanical Shock
- High Temperature Storage Test

Header Qualification

A component qualification was performed for the headers used in the PULSAR and PULSAR Max devices to ensure the supplier was capable of providing components that meet Guidant requirements. Thirty-two (32) units were tested. All units were found to operate according to specification. The following tests were performed during the qualification:

- Visual Inspection
- Dimensional Analysis
- Thermal Shock
- High Temperature/High Humidity Storage
- Methylenedianiline (MDA) Test
- Cytotoxicity

- Pyrogenicity
- Material Analysis

Electrical Design Verification Testing

The Electrical Design Verification Testing (DVT) was to verify the electrical requirements of the pulse generator (PG). These requirements included defibrillation requirements, Electromagnetic Interference (EMI), accelerometer, telemetry and battery requirements. Forty-one (41) units were tested. All units were found to operate according to specification.

Mechanical Design Verification Testing

The Mechanical DVT was performed to verify the mechanical requirements of the PG. This testing included dimensional analysis, hermeticity testing, and environmental and shipping tests. Thirty-four (34) units were tested. All units were found to operate according to specification.

System Design Verification Testing

The System DVT was performed to verify that previously established system requirements were met across subsystem interfaces, and to sample test requirements had been verified at lower levels. Pacing and sensing performance, sensor (accelerometer, minute ventilation, and blended) performance, therapy and diagnostic features, and pacing modes were tested as part of this DVT, using a fully integrated PG system (programmer, leads, pulse generator, magnet, physiologic simulation. In addition to the detailed verification testing of the System Features DVT on the superset model (model 1270), a subset of the features verification was performed on each of the PULSAR and PULSAR Max pacemaker models. Six (6) units were tested. All units were found to operate according to specification.

Software Design Verification Testing

The Software Design Verification Tests were performed to verify that the Model 2890 Software Application Requirements Specifications were met. The Software Application Requirements Specification specifies functional requirements of the software application, including windows behavior, telemetry communication, programming, interrogation, emergency functions, pulse generator model discrimination, and the "DEMO" mode. Twenty-eight (28) units were tested. All units were found to operate according to this specification.

Firmware Design Verification Testing

The Firmware DVT was performed to verify PG operating code and the firmware-to-hardware interface. Results of the DVT demonstrate that the PG firmware meets the design requirements. Four (4) units were tested. All units were found to operate according to specification.

Reliability Prediction

This analysis determined the predicted failure rates related to component performance, manufacturing process, and user environment. The method used is based on military standard MIL-HDBK-217F. Failure rates were compared with established Guidant reliability requirements to ensure they do not exceed the maximum requirements.

Failure Modes Effects and Criticality Analysis

The FMECA was performed as a bottom-up analysis. Components were analyzed and their failure effects assessed using a prescribed analysis method. When a failure mode was identified which would be likely to adversely affect safety or effectiveness, appropriate modifications were initiated to eliminate or minimize the failure cause and/or effect. These modifications included changes to design, test, and processes.

Sterilization Testing

Sterilization studies have been completed, and include Sterilization Equivalency, Sterilization Validation, Packaging Study (Accelerated), Sterilization Report for the Getinge Sterilizers, and Validation Report for Cosmed Contract Sterilizer. The analysis considered device construction/complexity/configuration, device packaging, sterilization load configuration/product density, load temperature/moisture, device cycle compatibility (review of materials used in the device), and aeration/EtO residuals. The Sterilization Validation Report verifies that the processes used in manufacturing PULSAR family devices produce devices which meet Guidant requirements for bioburden limits, pyrogen levels, and cytotoxicity. Test results demonstrated that the processes used to manufacture the PULSAR family devices meet bioburden, pyrogen, and cytotoxicity requirements. Validation testing was performed periodically at both the St. Paul (MN) and Cosmed (IL) sterilization facilities to demonstrate that the sterilization process is reproducible, capable of achieving a sterility assurance level (SAL) of 10^{-6} or better, and does not adversely impact device safety or effectiveness. Nine (9) units were tested. All units were found to operate according to specification.

Packaging Study, Accelerated

The Packaging Study was performed to ensure that the packaging design for the PULSAR family devices can withstand production processing, sterilization, packaging, shipping, and one-year shelf life (via an accelerated package aging). The testing included microbial challenge (to ensure packaging continues to provide a sterile barrier) and a lid/tray peel test (to verify a consistent heat seal bond).

Electromagnetic Interference Testing

In-vitro RF ablation testing was performed to verify that RF ablation energies do not interfere with the Reset function or cause the device to change pacing mode. An RF near field test was performed to verify correct operation of the pacemakers in the presence of RF energies at typical cell phone frequencies and with a pulse modulation scheme which is worst case for the PG. Specifically, the test showed that cell phone frequencies do not interfere with the reset function of the PULSAR devices or cause the sensing/pacing configuration to change modes. An Electronic Article Surveillance (EAS) test was performed to verify that EAS systems that were tested do not cause permanent changes in pacemaker performance. Specifically, that the EAS systems do not interfere with the reset function of PULSAR

devices and that the lead configuration function operates correctly if reset does occur. Twelve (12) units were tested. All units were found to operate according to specification.

Biocompatibility

A biocompatibility assessment was conducted to verify that the materials used in the PULSAR family of pacemakers are biocompatible. The assessment included reviewing the effects of manufacturing processes on the materials.

The tissue-contacting materials used in the PULSAR and PULSAR Max pulse generators are the same as those used in commercially available pulse generators (e.g. VIGOR), and the manufacturing processes are similar. These materials and processes have been previously tested to ensure biocompatibility. Materials include polyurethane, platinum cured silicone rubber, titanium, 316L stainless steel, and medical adhesive. Biocompatibility evaluation on these materials was performed in accordance with the Guidant Material Biocompatibility Evaluation Procedure SOP5088, which is based upon ISO 10993-1: 1994 Biological Evaluation of Medical and Dental Materials and Devices, Part 1: Guidance on Selection of Tests. Because previous testing covers these materials, no additional biocompatibility testing was necessary.

9.2 Animal Implant Studies

The objective of the animal implant study was to demonstrate that the pacemaker system functions appropriately under various challenges in a simulated clinical setting. Test situations that are likely to arise during human implantation and follow-up were simulated using canines in this study. The tests included measuring *in vivo* cardiac signals, demonstrating various diagnostic and MV therapy features, and verifying satisfactory operation during post-surgical follow-up.

9.3 Simulated Use Testing

This test evaluated the pacemaker system in a simulated clinical/field environment. Testing included reviewing the user instructions for accuracy/clarity, and performing simulated clinical scenarios to ensure the pacemaker system performs as intended. Testing was performed on PULSAR Max pacemakers. Five (5) units were tested. All units were found to operate according to specification.

Atrial Flutter Response

An Atrial Flutter Response (tape) test was performed to verify that the feature (AFR) works as intended when presented with physiologic atrial waveforms. The test was conducted using previously recorded human arrhythmic episodes.

9.4 Accelerometer Equivalency Testing

Bench and paired device human exercise testing were performed to demonstrate that the accelerometer adaptive-rate behavior of the PULSAR and PULSAR Max pacemakers is equivalent to the adaptive-rate behavior of commercially available VIGOR pacemakers (P940031, approved 6/95).

Bench testing consisting of an off-axis Design Analysis Test was conducted to evaluate whether accelerometer rate response is linear and is sensitive to the same amplitude, frequency of acceleration, and axis of motion as the commercially available VIGOR. Ten (10) units were tested and met all test requirements

A human exercise test was performed to confirm equivalent behavior of the accelerometer adaptive-rate response under actual conditions of human activity. This test involved externally attaching both the PULSAR and VIGOR devices to human test subjects. The test subjects then performed routine physical activity consisting of a 12 minute hall walk. During these activities, sensor-indicated rate was stored by both devices. The sensor-indicated rates provided by the two devices were then compared to ensure equivalent performance per specified acceptance criteria.

9.5 Conclusion Concerning Nonclinical Laboratory Tests

All nonclinical evaluation and test results were found to be acceptable.

10 Summary of Clinical Studies

A clinical study was conducted using PULSAR Max devices per the protocol approved under Product Development Protocol (PDP) D970003. Enrollment was initiated on June 15, 1998, and completed on September 9, 1998 with a total of 130 patients implanted at 28 investigational centers. The average implant duration was 5.8 months with a maximum implant duration of 7.2 months and a total cumulative implant experience of 754 device months. The mean age of patients implanted with this device was 67.5 years, with a standard deviation of 13.2 years.

10.1 Objectives

The objectives for the PULSAR Max investigational study are summarized below.

Primary Endpoint 1: Sensor Indicated Rate (SIR) Slope Response
The acceptance criterion for this endpoint was defined as the slope between the SIR and Expected Heart Rate (HER) were equivalent to 1 if the 95% CI of the slope is between $\subset$ [0.65, 1.35].

Primary Endpoint 2: Complication Rate
The acceptance criterion for this endpoint was that the 3-month complication rate was less then or equal to 14.6% (i.e. no more than 19 out of 130 patients) having a complication.

Secondary Endpoint 1: Atrial Flutter Response (AFR)
An inappropriate device response to the AFR feature was defined as the device having any of the following events: 1) Device fails to switch to VDI(R) (only available in DDD(R) and DDI(R)) pacing after an atrial flutter event (rate > than 230 bpm/min) captured by the Holter monitor, or 2) Device mode switches without an atrial flutter event captured by the Holter monitor.

The acceptance criterion for this endpoint was defined as an inappropriate response rate of zero (0). The failure criterion for this endpoint was defined as one or more inappropriate occurrences.

Secondary Endpoint 2: AV Search Hysteresis
An inappropriate device response to the AV Search Hysteresis feature was defined as a device failing to increase the AV conduction period beyond the programmed AV delay time, but within the programmed AV Search Hysteresis time. The search event was observed on every device with an ECG during the AV Search Hysteresis evaluation at the pre-discharge follow-up.

The acceptance criterion for this endpoint was defined as an inappropriate response rate of zero (0). The failure criterion for this endpoint was defined as of one or more inappropriate occurrences.

Secondary Endpoint 3: Dynamic PVARP
An inappropriate device response to the Dynamic PVARP feature was defined as a device failing to achieve the maximum tracking rate at the maximum exercise stage during either CAEP Exercise test, while having the PVARP set at a resting rate.

The acceptance criterion for this endpoint was defined as an inappropriate response rate of zero (0). The failure criterion for this endpoint was defined as of one or more inappropriate occurrences.

Secondary Endpoint 4: Fix Baseline During Exercise
An inappropriate device response to the Fix Baseline During Exercise feature verified during daily activity was defined as a physician noticed inappropriate pacing events on the Holter monitor report.

The acceptance criterion for this endpoint was defined as an inappropriate response rate of zero (0). The failure criterion for this endpoint was defined as of one or more inappropriate occurrences.

Secondary Endpoint 5: Automatic Response Factor
The inappropriate device response to the Automatic Response Factor feature was defined as the device having the following events: 1) accelerometer response factor changed more than 6% of the previous value or MV response factor changed more than 4% of the previous value; 2) cumulative changes (entire programmable range from programmed value) in accelerometer response factor value greater than 20% of the cumulative changes and when the MV response factor value greater than 30% of cumulative change.

The acceptance criterion for this endpoint was defined as an inappropriate response rate of zero (0). The failure criterion for this endpoint was defined as of one or more inappropriate occurrences.

10.2 Methods

A total of 130 patients were implanted with the dual chamber (DR) PULSAR Max pacemaker in a controlled, prospective study. The investigator was responsible for screening all potential patients and selecting those who were appropriate for study inclusion. The patients selected for participation were from the investigator's general patient population meeting the indications for use of the PULSAR Max pacemaker. Patients with an implantable cardioverter defibrillation (ICD) or who were candidates for an ICD implant were excluded from the investigation. Each patient was followed at hospital discharge and at one and three months post-implant. The pre-discharge follow-up included a low intensity treadmill exercise (LITE) for sensor optimization and 24 hour Holter monitoring. Fifty-five (55) patients underwent additional testing consisting of Holter monitoring and repeated treadmill testing at the one-month follow-up visit utilizing the low intensity treadmill exercise protocol (LITE) and Chronotropic Assessment Exercise Protocol (CAEP) tests. The investigation was conducted at 13 U.S. centers and 15 European centers. To prevent imbalance of treadmill testing experience among the participating centers all treadmill tests were performed in the U.S.

Table 2. Patient Population Characteristics

Characteristic	Number
Age at Implant (years)	
Minimum	18.2
Maximum	92.2
Mean	67.5
Standard Deviation	13.2
Gender (# of patients, %)	
Male	81 (62.3%)
Female	49 (37.7%)

Table 3. Patient Arrhythmia History

Arrhythmias*	Number of subjects
Sinus Bradycardia	40
Sinus Arrhythmia	1
Paroxysmal Atrial Fibrillation	27
Atrial Fibrillation (AF) (Chronic)	1
Atrial Flutter	4
PSVT	3
PAT	5
Sinus Arrest	6
Sinus Node Dysfunction (Brady-Tachy Synchrony)	21
1st - Degree AV Heart Block	19
2nd - Degree AV Block (Mobitz 1)	6
2nd - Degree AV Block (Mobitz 11)	18
3rd - Degree AV Block	33
Left Bundle Branch Block	6
Right Bundle Branch Block	11
Arrhythmia Resulting from Ablation	4
Intraventricular Conduction Delay	1
Other	23

(*Numbers may not be summed as some patients may be reported in more than one category.)

Table 4 below summarizes the programmed parameters for patients who performed CAEP exercise testing.

Table 4. Programmed Parameters During CAEP Testing
(n=55)

Brady Parameter	Mean	Standard Deviation	Minimum	Maximum
Lower Rate Limit	64	6.5	55	80
Maximum Sensor Rate	151	16.0	100	185
MV Rate Response Factor	5	1.7	3	11

The Expected Heart Rate (EHR) and the Sensor Indicated Rate (SIR) at each stage of exercise were used to generate a slope of response to graded exercise testing (CAEP), using the Wilkoff model. Sensor indicated rates of MV and Blended sensor were measured in repeated (two) identical CAEP treadmill tests with MV or Blended sensor turned on. The EHR slope and the observed SIR slope responses were then compared. A slope of 1.0 was the expected response. Overall device safety and appropriate performance of the enhancement features were evaluated when the device was assigned to either the MV-only or Blended sensor mode during the follow-up period.

10.3 Results

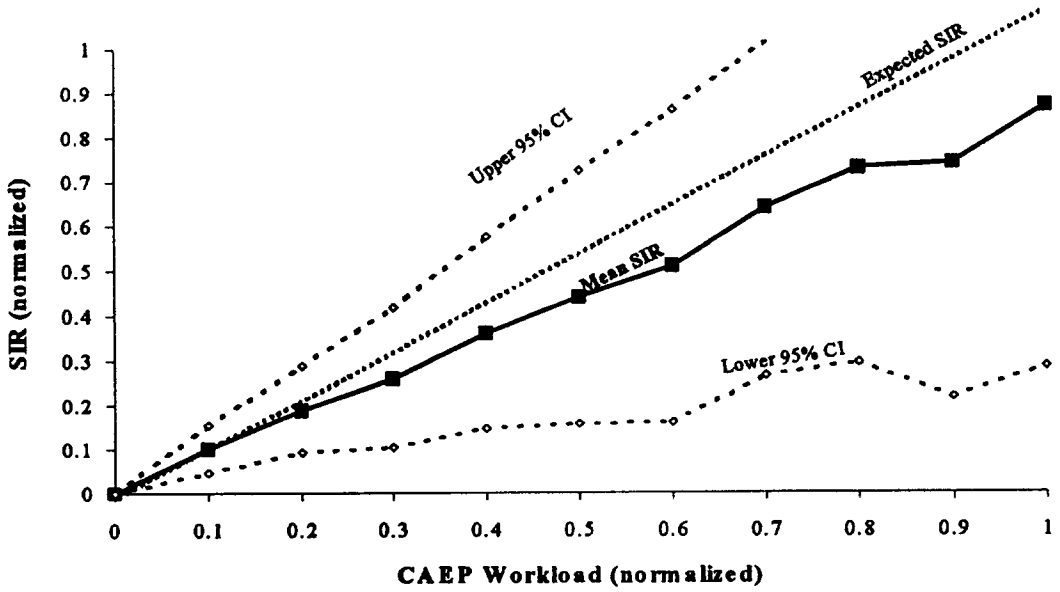
Primary Endpoint 1: SIR Slope Response

The mean sensor response slope during CAEP treadmill tests for patients programmed to the Minute Ventilation sensor only setting was 0.83 with 95% CI [0.74, 0.92]; mean sensor response slope for patients programmed to the Blended sensor setting was 0.81 with 95% CI [0.73, 0.89]. These values meet the acceptance criteria for this endpoint.

Table 5. Results of Exercise Testing – Total Clinical Population
(n=110 CAEPS total)

Population	n (% of pts)	Slope mean [95% CI]
Blended	51 (91%)	0.81 [0.73, 0.89]
MV Only	45 (83%)	0.83 [0.74, 0.92]

Figure 2. Sensor-indicated rate (SIR) vs expected rate during CAEP
(All patients completing at least four stages of exercise, blended sensor only (n=46, at 1 month))



Primary Endpoint 2: Complication Rate
The resulting complication rate was 10.8% of patients (14 out of 130) vs. the acceptance criterion of 14.6% of patients (19 out of 130). This value met the acceptance criterion for this endpoint.

Secondary Endpoint 1: Atrial Flutter Response (AFR)
No inappropriate responses were noted; this feature met the acceptance criterion for this endpoint.

Secondary Endpoint 2: AV Search Hysteresis
No inappropriate responses were noted; this feature met the acceptance criterion for this endpoint.

Secondary Endpoint 3: Dynamic PVARP
No inappropriate responses were noted; this feature met the acceptance criterion for this endpoint.

Secondary Endpoint 4: Fix Baseline During Exercise
No inappropriate responses were noted; this feature met the acceptance criterion for this endpoint.

Secondary Endpoint 5: Automatic Response Factor
37% of the response factor change was outside the predefined acceptance criteria for the minute ventilation auto response factor, and 5% of the accelerometer response factor change was outside the predefined criteria. Analysis of the data shows the feature to be working as expected; the variation in results was attributed to programming preferences not anticipated prior to the start of the investigation. FDA agrees that the feature worked as designed, and that the programming preferences of the physicians probably accounted for the changes being outside of the predefined criteria.

10.4 Gender Bias Analysis

Eighty-one males (62.3 %) and 49 females (37.7 %) were implanted within the PULSAR Max clinical investigation. No statistical differences were found between males and females implanted within the PULSAR Max with respect to age (p = 0.64 , t-test).

One death occurred among males. No statistical difference in all-cause mortality was found between males and females implanted with the study devices (p = 0.62, Fisher exact test). No peri-operative deaths occurred among females. Two peri-operative deaths occurred among males.

No statistical difference was found between males and females implanted with the PULSAR Max with respect to adaptive rate response slopes with the minute ventilation sensor (p = 0.29) or the blended sensor (p = 0.19).

The results between males and females show that safety and efficacy do not differ with respect to gender.

11 Conclusions Drawn from the Studies

The preclinical testing demonstrates that the PULSAR/PULSAR series pacemakers operate according to system performance specifications.

The clinical data support the following conclusions regarding the safety and efficacy of the PULSAR/PULSAR Max series pacemakers:

- The PULSAR/PULSAR Max met the primary efficacy endpoint acceptance criteria for SIR sensor response, and met the primary safety endpoint criteria for complication rate.
- The PULSAR/PULSAR Max met the secondary feature acceptance criteria for Atrial Flutter Response, AV Search Hysteresis, Dynamic PVARP, and Fix Baseline During Exercise, and demonstrated acceptable performance for the secondary endpoint for Automatic Response Factor.
- The PULSAR/PULSAR Max CAEP data demonstrate that the sensor indicated rates in the overall population are proportional to increasing workload in a linear fashion as seen in the normal heart rate to workload relationship.

In accordance with the above conclusions, the clinical data provides reasonable assurance that the PULSAR/PULSAR Max series pacemakers are safe and effective for the treatment of conditions requiring chronic cardiac pacing as specified in Section 2.0, under the proposed conditions of use.

12 Panel Recommendation

The Circulatory Panel recommended approval of the PDP protocols on December 4, 1997.

13 FDA Decision

FDA waived the GMP inspection for the PULSAR because of a previous inspection (June 23, 1998) of the same manufacturing facility for a related device, with no reported observations.

14 Approval Specifications

Directions for Use: See Final Draft Labeling (Information for Use)

Hazards to Health from Use of the Device: See INDICATIONS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE EVENTS in the Final Draft Labeling (Information for Use).

Post-approval Requirements and Restrictions:

Approval was conditioned on Guidant addressing two performance-related issues that occurred during device development.

14.1 Recall for Short Circuit/ Rapid Battery Depletion

Discovery/Meridian pacemakers manufactured in July, August and September, 1998, were recalled due to rapid battery depletion. The Discovery/Meridian pacemakers are commercially available devices built with identical components as the PULSAR. The problem is associated with three IC's packaged together in what Guidant calls a "triple pack", and is believed to occur when an IC is misaligned allowing wires from two IC's to touch.

There have been 20 confirmed failures, and there are 9103 devices that may be affected. Device failure may be manifest by: no telemetry, pacing in backup mode and no output. A recall plan, "Dear Doctor" letter and corrective action (visual inspection of the triple stack) have all been approved by the Minneapolis District Office.

Although FDA believes that the steps taken thus far provide a reasonable assurance of the safety of the pulse generators, there was still some concern that the visual inspection alone was not adequate to address the problem. Therefore, as a condition of approval, Guidant was required to report monthly on any failures for rapid battery depletion, and submit a supplement for a permanent fix or some other mutually agreeable solution within six months.

14.2 High Rate Pacing-Clinical presentation

To address the problem of inappropriate sustained high rate pacing (discussed in section 8 above) a "Warning" will be included in the labeling. (See the first warning in Section 4, Warnings and Precautions).

Within 90 days of the date of this letter, Guidant must submit a PDP supplement to eliminate the MV auto-initialization feature. MV calibration will be limited to the manual 4-ON method only. Physician's manual and other labeling must be modified as needed to provide the new configuration information. The Model 2890 software application must be modified to have the above referenced Minute Ventilation (MV) Calibration Warning appear as a "pop-up" message before the 4-ON calibration screen is entered.

See Approval Order for additional Conditions of Approval